



## GLUT1 deficiency syndrome

GLUT1 deficiency syndrome is a disorder affecting the nervous system that can have a variety of neurological signs and symptoms. Approximately 90 percent of affected individuals have a form of the disorder often referred to as common GLUT1 deficiency syndrome. These individuals generally have frequent seizures (epilepsy) beginning in the first months of life. In newborns, the first sign of the disorder may be involuntary eye movements that are rapid and irregular. Babies with common GLUT1 deficiency syndrome have a normal head size at birth, but growth of the brain and skull is often slow, which can result in an abnormally small head size (microcephaly). People with this form of GLUT1 deficiency syndrome may have developmental delay or intellectual disability. Most affected individuals also have other neurological problems, such as stiffness caused by abnormal tensing of the muscles (spasticity), difficulty in coordinating movements (ataxia), and speech difficulties (dysarthria). Some experience episodes of confusion, lack of energy (lethargy), headaches, or muscle twitches (myoclonus), particularly during periods without food (fasting).

About 10 percent of individuals with GLUT1 deficiency syndrome have a form of the disorder often known as non-epileptic GLUT1 deficiency syndrome, which is usually less severe than the common form. People with the non-epileptic form do not have seizures, but they may still have developmental delay and intellectual disability. Most have movement problems such as ataxia or involuntary tensing of various muscles (dystonia); the movement problems may be more pronounced than in the common form.

Several conditions that were originally given other names have since been recognized to be variants of GLUT1 deficiency syndrome. These include paroxysmal choreoathetosis with spasticity (dystonia 9); paroxysmal exercise-induced dyskinesia and epilepsy (dystonia 18); and certain types of epilepsy. In rare cases, people with variants of GLUT1 deficiency syndrome produce abnormal red blood cells and have uncommon forms of a blood condition known as anemia, which is characterized by a shortage of red blood cells.

### Frequency

GLUT1 deficiency syndrome is a rare disorder. Approximately 500 cases have been reported worldwide since the disorder was first identified in 1991. In Australia, the prevalence of the disorder has been estimated at 1 in 90,000 people. However, researchers suggest that the disorder may be underdiagnosed, because many neurological disorders can cause similar symptoms.

## Genetic Changes

GLUT1 deficiency syndrome is caused by mutations in the *SLC2A1* gene. This gene provides instructions for producing a protein called the glucose transporter protein type 1 (GLUT1). The GLUT1 protein is embedded in the outer membrane surrounding cells, where it transports a simple sugar called glucose into cells from the blood or from other cells for use as fuel.

In the brain, the GLUT1 protein is involved in moving glucose, which is the brain's main energy source, across the blood-brain barrier. The blood-brain barrier acts as a boundary between tiny blood vessels (capillaries) and the surrounding brain tissue; it protects the brain's delicate nerve tissue by preventing many other types of molecules from entering the brain. The GLUT1 protein also moves glucose between cells in the brain called glia, which protect and maintain nerve cells (neurons).

*SLC2A1* gene mutations reduce or eliminate the function of the GLUT1 protein. Having less functional GLUT1 protein reduces the amount of glucose available to brain cells, which affects brain development and function.

## Inheritance Pattern

This condition is usually inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. About 90 percent of cases of GLUT1 deficiency syndrome result from new mutations in the gene. These cases occur in people with no history of the disorder in their family. In other cases, an affected person inherits the mutation from an affected parent.

In a small number of families, GLUT1 deficiency syndrome is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

## Other Names for This Condition

- De Vivo disease
- encephalopathy due to GLUT1 deficiency
- G1D
- glucose transport defect, blood-brain barrier
- glucose transporter protein syndrome
- glucose transporter type 1 deficiency syndrome
- Glut1 deficiency

- GLUT1 DS
- GTPS

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Glucose transporter type 1 deficiency syndrome  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847501/>

### Other Diagnosis and Management Resources

- G1D Registry  
<https://www.g1dregistry.org/>
- GeneReview: Glucose Transporter Type 1 Deficiency Syndrome  
<https://www.ncbi.nlm.nih.gov/books/NBK1430>
- The Glucose Transporter Type 1 Deficiency Syndrome Research Consortium (G1DRC)  
<http://www.utsouthwestern.edu/education/medical-school/departments/neurology/programs/rare-brain-disorders/g1drc.html>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

## **Additional Information & Resources**

### MedlinePlus

- Health Topic: Carbohydrate Metabolism Disorders  
<https://medlineplus.gov/carbohydratemetabolismdisorders.html>
- Health Topic: Genetic Brain Disorders  
<https://medlineplus.gov/geneticbraindisorders.html>

### Genetic and Rare Diseases Information Center

- Glucose transporter type 1 deficiency syndrome  
<https://rarediseases.info.nih.gov/diseases/9265/glucose-transporter-type-1-deficiency-syndrome>

### Educational Resources

- Disease InfoSearch: Glucose Transport Defect, Blood-Brain Barrier  
<http://www.diseaseinfosearch.org/Glucose+Transport+Defect%2C+Blood-Brain+Barrier/3098>
- MalaCards: glut1 deficiency syndrome 1  
[http://www.malacards.org/card/glut1\\_deficiency\\_syndrome\\_1](http://www.malacards.org/card/glut1_deficiency_syndrome_1)
- Orphanet: Encephalopathy due to GLUT1 deficiency  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=71277](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=71277)

### Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases  
<http://www.climb.org.uk/>
- Glut1 Deficiency Foundation  
<http://www.g1dfoundation.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/glucose-transporter-type-1-deficiency-syndrome/>
- RareConnect  
<https://www.rareconnect.org/en/community/glut1-ds>

### GeneReviews

- Glucose Transporter Type 1 Deficiency Syndrome  
<https://www.ncbi.nlm.nih.gov/books/NBK1430>

### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22GLUT1+deficiency+syndrome%22>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28glut1+deficiency+syndrome%5BTIAB%5D%29+OR+%28glucose+transporter+protein+syndrome%5BTIAB%5D%29+OR+%28glucose+transporter+type+1+deficiency+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D>

## OMIM

- GLUT1 DEFICIENCY SYNDROME 1  
<http://omim.org/entry/606777>

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